Oral features in Kabuki make-up Syndrome

G. SPANO, G. CAMPUS, A. BORTONE, V. LAI, P.F. LUGLIÈ

Abstract

Aim Kabuki make-up Syndrome is so named because of the characteristic facies of the affected patient. The face is similar to a Kabuki actor’s mask. The main aim of this report was to describe the oral features in Kabuki Syndrome, focusing on the tooth anomalies. Patients and methods Five subjects with Kabuki Syndrome, identified by the Child Neuropsychiatric Clinic of the University of Sassari, Italy, were enrolled. Their medical records were reviewed and oral and dental examinations were completed. The diagnosis was based upon the typical pattern of malformations and dysmorphic features reviewed by Matsumoto and Niikawa. Results All patients showed typical characteristics of the Syndrome such as a long palpebral fissure, lower palpebral eversion, arched eyebrows, short nasal septum, prominent and large ears, fingertip pads, mental retardation, and paramedian elevation of the lower lip. Conclusion Kabuki make-up Syndrome is of unknown origin but a genetic aetiopathogenesis has been proposed. It is extremely rare; in Japan, where it is most frequent, it affects 1:32000 newborns. The typical facies of the syndrome, combined with general medical and dental examinations, are very important for diagnosis confirmation.

Keywords: Kabuki make up Syndrome; Oral features; Hypodontia; Ogival palate.

Introduction

Kabuki make-up Syndrome is so named because of the characteristic facies of the affected patient. The face is similar to a Kabuki actor’s mask, which was traditionally used in the Japanese theatre during the Edo period (1603-1867). This syndrome is a multiple congenital anomaly/mental retardation syndrome that was first described simultaneously by two groups in Japan [Niikawa et al., 1981; Kuroki et al., 1981]. The authors reported a group of patients who showed characteristic facial features, skeletal anomalies, dermatoglyphic abnormalities, short stature and mental retardation. The frequency is about 1:32000 in Japan [Niikawa et al., 1988]. In 1988, 62 cases were described, 58 from Japan. Based on the findings in these patients, the following five cardinal manifestations were defined [Niikawa et al., 1988].

1. All patients exhibited the characteristic facies, with eversion of the lower eyelids to the bottom, curved eyebrow, flat nose and prominent ears.
2. In 92% of the examined sample, skeletal anomalies were recorded such as a deformed spinal column with or without sagittal cleft vertebrae and brachydactyly V.
3. Dermatoglyphic anomalies (fingertip pads, absence of digital triradius c and/or d, and increased digital ulnar loop and hypothenar loop patterns) were described in 93% of the patients.
4. A growth deficit was observed in most of the patients (83%) with normal birth and normal weight at birth.
5. Cardiac anomalies were observed in one third of the examined cases.

Similar features have also been described in other studies, not carried out in Japan, where this syndrome is more common than originally supposed [Braun and Schmid, 1984; PeBenito and Ferretti, 1989; Gillis et al., 1990; Philip et al., 1992; Burke and Jones, 1995; Ilyina et al., 1995; Ho and Eaves, 1997; Kokitsu-Nakata et al., 1999; Courtens et al., 2000]. A recent report [White et al., 2004] estimates a frequency rate of 1:86000 in Australia and New Zealand. However, the real frequency of the syndrome is under scrutiny and it is probably similar to that observed in Japan [Adam and Hudgins, 2005]. Several studies have described the main oral characteristics of Kabuki Syndrome. Common manifestations are ogival palate, labio-palatal cleft, dental form anomalies, and hypodontia ranging 2.8% - 7.4% in the permanent dentition, less frequent in the deciduous dentition [Balmer et al., 2001; Matsumoto...
and Niikawa, 2003]. No gender difference was observed, but an aetiopathogenic hypothesis has linked transmission of the syndrome to the X chromosome [Niikawa et al., 1988; Li et al., 1996].

The most widely-accepted aetiopathological hypothesis postulates a hereditary pathological syndrome with dominant autosomal transmission, in which each new case is a new mutation [Niikawa et al., 1988].

There are no published data about the prevalence of the syndrome in Italy; the aim of this report is to describe the oral features in Kabuki Syndrome, focusing on the tooth anomalies.

**Patients and methods**

**Clinical evaluation**

Five individuals (Fig. 1) with Kabuki Syndrome, identified by the Child Neuropsychiatric Clinic of the University of Sassari, Italy, agreed to participate in the study. No similar signs were observed in any of the families of the patients, indicating sporadic occurrence. Medical records were reviewed and oral and dental examinations were performed. The diagnosis was based upon the typical pattern of malformations and dysmorphic features (Table 1) [Matsumoto and Niikawa, 2003].

Dental examinations were carried out under standard conditions with plane mirror and dental probe. Dental anomalies such as conoid teeth and agenesis were also recorded. Occlusion status was classified following IOTN grading.

**Clinical reports**

**Patient 1**

A girl born in 1998 after a normal term pregnancy and normal delivery with a birth weight of 2900 g. Impaired growth was observed at three months. Impaired psychomotor development was detected at the age of 23 months. A moderately severe heart defect was diagnosed at 25 months. The girl attends a special-needs school. Dental anomalies of 31 and 41 (hypoplasia), agenesia of 12, 22, 25, 32, 35, 45. The maxilla was retrognathic. Several caries lesions were noted. Anterior cross-bite and ogival palate.

**Patient 2**

A girl born in 1992 at the 38th week with normal delivery and a birth weight of 2750 g, after a pregnancy with continuous risk of miscarriage. Psychomotor development was delayed. The girl attends a special-needs school. Dental anomalies of 11 and 21 with a flat screwdriver-like crown, with white spots and hypoplasia; the upper left second incisor showed a conical shaped crown; agenesia of 12, 14, 31, 41. Several caries lesions observed. Bilateral cross-bite and ogival palate.

**TABLE 1** - Vital statistics (age and gender) and main features of the five patients.
Patient 3
A boy born in 1994 at the 33th week with caesarean delivery and a birth weight of 1450 g, after a pregnancy with continuous risk of miscarriage. At birth the patient was reanimated. Impaired growth was observed at three months. Impaired psychomotor development was detected at 36 months. Dental anomalies of 11 and 21, agenesis of 12, 22, 31, 42, 44. Several caries lesions observed. Left lateral cross-bite and ogival palate (fig. 2).

Patient 4
A boy born in 1986 after a normal term pregnancy and normal delivery with a birth weight of 3480 g. Growth deficiency was observed at six months. Impaired psychomotor development was detected at 11 months. A moderately severe heart defect was diagnosed at 18 months. The boy attends a special-needs school. Dental anomalies and enamel hypoplasia of 11 and 21, the upper second incisors displayed a conical shaped crown; agenesis of 45. Several caries lesions observed. Bilateral cross-bite and ogival palate.

Patient 5
A girl born in 1991 after a normal term pregnancy and normal delivery, birth weight 3800 g. Growth deficiency was diagnosed at 3 years of age. Impaired psychomotor development was detected at 45 months. The girl attends a special-needs school. Enamel hypoplasia of 11 and 21 was observed. Several caries lesions observed. Anterior cross-bite and ogival palate.

Discussion
The aim of this investigation was to describe the main oral and dental features in patients with Kabuki Syndrome. This is a multiple malformation/mental retardation syndrome characterised by distinctive facial features (eversion of the lower lateral eyelid, arched eyebrows with the lateral one-third dispersed or sparse, depressed nasal tip and prominent ears), skeletal anomalies, dermatoglyphic abnormalities including persistent fingertip pads, mild to moderate mental retardation, and postnatal growth deficiency. It is extremely rare; in Japan, where it is most frequent, it affects 1:32000 new births. Dental anomalies are commonly described in Kabuki Syndrome patients: over 70% of the affected ones [Adam and Hudgins, 2005]; hypodontia is recorded in about 40% of Kabuki patients [Lerone et al., 1997]. These clinical features may be helpful in the diagnostic process to identify mildly affected carrier parents.

The findings confirm the principal characteristics of the syndrome: long palpebral fissure, lower palpebral eversion, arched eyebrows, short nasal septum, prominent and large ears, fingertip pads, mental retardation, and paramedian elevation of the lower lip.

Cardiac problems are found in almost 50% of the affected subjects. Recently several papers report that Kabuki’s patients could be more prone to many general medical problems like obesity and diabetes mellitus [Fujishiro et al., 2003; Shalev et al., 2004; White et al., 2004]. Therefore, it is essential that patients and caregivers be aware of signs of these diseases. Kabuki Syndrome might be associated by a weakened immune system.
system, indicating therefore a high risk of infection [Niikawa et al., 1988; Matsumoto and Niikawa, 2003; Atar et al., 2006].

Two of the patients described in this report showed cardiac problems. It should be emphasised that the existence of congenital cardiac abnormalities in Kabuki patients makes them at high risk for bacterial endocarditis and therefore administration of a prophylactic antibiotic regimen before invasive dental procedures is a highly advisable approach [dos Santos et al., 2006].

Kabuki patients show mental retardation (from mild to moderate) but they are usually self-sufficient and with a good life skills, so they have been reported with a relatively high level of collaboration, good memory, friendly temperaments [White et al., 2004].

Regarding the oral and dental features, hypodontia and associated wide spaces between teeth were observed in patients 1, 2, 3 and 4. No tooth buds were recorded for the lower incisors or upper lateral incisors [Niikawa et al., 1981; Kuroki et al., 1981; Niikawa et al., 1988; Gillis et al., 1990; Philip et al., 1992]. One of the findings of particular concern was the very poor oral hygiene status and evidence of EEC detected in all our patients.

In the province of Sassari (Sardinia, Italy) the population is estimated to be 300,000 inhabitants, of which 56,831 [www.istat.it] in the age range of the examined sample (9-20 years), so the estimated prevalence of Kabuki Syndrome is 1:11600.

**Conclusion**

Oral/dental features in Kabuki patients could play an important role in the understanding of the pathogenesis of this syndrome. The contribution of dental professionals can support and help the diagnosis of this condition, and facilitate referral to a clinical geneticist and to the practitioner responsible for the comprehensive care of these patients.

**References**


Italian Nation Institute of Statistics (ISTAT) [www.istat.it]


